

CLAIMS

1 *Sub C1* 1. A method for production of an autologous vaccine to tumor cells
2 comprising transducing the tumor cells with one or more species herpes simplex virus
3 amplicon containing the gene for an immunomodulatory protein and at least one additional
4 therapeutic gene to provide transient expression of the immunomodulatory protein and the
5 therapeutic gene product by the cells.

1 2. The method according to claim 1, wherein the tumor cells are
2 transduced with the herpes simplex amplicons *ex vivo*.

1 3. The method according to claim 1, wherein the tumor cells are
2 transduced with the herpes simplex cell *in vivo*.

1 *Sub C1* 4. A method for inducing a protective immune response to tumor cells
2 in a patient comprising the step of transducing the tumor cells with one or more species
3 herpes simplex virus amplicon containing the gene for an immunomodulatory protein and at
4 least one additional therapeutic gene to provide transient expression of the
5 immunomodulatory protein and the therapeutic gene product by the cells.

1 5. The method according to claim 4, wherein the tumor cells are
2 transduced with the amplicon *ex vivo*, further comprising the step of introducing the
3 transduced tumor cells into the patient.

1 6. The method according to claim 4, wherein the amplicons are injected
2 into the site of the tumor cells *in vivo*.

2 *Sub C1* 7. The method according to ~~any of claims 1 to 6~~, wherein the
2 immunomodulatory protein is a cytokine.

1 8. The method according to claim 7, wherein the cytokine is
2 interleukin-2.

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1 9. The method according to claim 7, wherein the cytokine is granulocyte-
2 macrophage colony stimulating factor.

1 *Sub C1* 10. The method according to claim 7, wherein the immunomodulatory
2 protein is a chemokine.

1 11. The method according to claim 10, wherein the chemokine is
2 RANTES.

1 *Sub C1* 12. The method according to ~~any of claims~~ claim 1 to 6, wherein the
2 immunomodulatory protein is a intercellular adhesion molecule.

1 13. The method according to claim 12, wherein the intracellular adhesion
2 molecule is ICAM-1.

1 *Sub C1* 14. The method according to ~~any of claims~~ 1 to 6, wherein the
2 immunomodulatory protein is a costimulatory factor.

1 15. The method according to claim 14, wherein the costimulatory factor
2 is B7.1.

1 *Sub C1* 16. The method according to ~~any of claims~~ 1 to 15, wherein a population
2 of tumor cells is transduced with a plurality of species of amplicons containing the genes for
3 the immunomodulatory protein and the additional therapeutic gene.

1 17. The method according to ~~any of claims~~ 1 to 16, wherein the
2 additional therapeutic gene encodes a second immunomodulatory protein.

1 18. The method according to ~~any of claims~~ 17, wherein the tumor cells
2 are transduced with amplicons encoding and expressing at least two species of cytokines.

1 19. The method according to claim 18, wherein tumor cells are
2 transduced with amplicons containing the genes for interleukin-2 and interleukin-12.

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1 20. The method according to claim 18, wherein the tumor cells are
2 transduced with amplicons encoding and expressing a cytokine and a costimulatory factor.

1 21. The method according to claim 20, wherein tumor cells are
2 transduced with amplicons containing the genes for RANTES and B7.1.

1 *a* 22. The method according to ~~any of claims 1-21~~, wherein the tumor cells
2 are hepatoma cells or lymphoma cells.

1 *Sub C1* 23. A mixture containing a plurality of species of herpes simplex virus
2 amplicons, including at least a first species of amplicon containing the gene for at least one
3 immunomodulatory protein and a second species of amplicon containing the gene for an
4 additional therapeutic gene product.

1 24. The mixture according to claim 23, wherein the immunomodulatory
2 protein is a cytokine.

1 25. The mixture according to claim 24, wherein the cytokine is
2 interleukin-2 or granulocyte macrophage colony stimulating factor.

1 *Sub C1* 26. The mixture according to claim 23, wherein the immunomodulatory
2 protein is a chemokine.

1 27. The mixture according to claim 26, wherein the chemokine is
2 RANTES.

1 *Sub C1* 28. The mixture according to claim 23, wherein the immunomodulatory
2 protein is an intercellular adhesion molecule.

1 29. The mixture according to claim 28, wherein the intracellular adhesion
2 molecule is ICAM-1.

1 *Sub C1* 30. The mixture according to claim 23, wherein the immunomodulatory
2 protein is a costimulatory factor.

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1 31. The mixture according to claim 30, wherein the costimulatory factor
2 is B7.1.

1 *Sub C1* 32. The mixture according to ~~any of claims~~ claim 23 ~~31~~, wherein the
2 additional therapeutic gene encodes a second immunomodulatory protein.

1 33. The mixture according to ~~any of claims~~ claim 23 ~~32~~, wherein the
2 first and second species of amplicons contains genes encoding for RANTES and B7.1.

1 34. The mixture according to ~~any of claims~~ claim 23 ~~32~~, wherein the
2 first and second species of amplicons contains genes encoding for at least two species of
3 cytokines.

1 35. The mixture according to claim 34, wherein the amplicons contain
2 genes encoding for interleukin-2 and interleukin-12.

1 36. Tumor cells transduced in accordance with the methods of ~~any of~~
2 ~~claims 1 to 22~~.

1 37. Tumor cells transduced with a mixture of herpes simplex virus
2 amplicons in accordance with ~~any of claims~~ 23 ~~to 35~~.

1 *Sub C1* 38. A method for production of an autologous vaccine to tumor cells
2 comprising transducing the tumor cells with a herpes simplex virus amplicon containing the
3 gene for an immunomodulatory protein to provide transient expression of the
4 immunomodulatory protein by the cells, wherein the immunomodulatory protein is selected
5 from among chemokines, intercellular adhesion molecules and costimulatory factors.

1 39. The method according to claim 1, wherein the tumor cells are
2 transduced with the herpes simplex amplicons *ex vivo*.

1 40. The method according to claim 1, wherein the tumor cells are
2 transduced with the herpes simplex cell *in vivo*.

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